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PTO/SB/21 (05-03)
Approved for use through 04/30/2003. OMB 0651-0031
U.S. Patent and Trademark Office; U.S. DEPARTMENT OF COMMERCE
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TRANSMITTAL FORM

(to be used for all correspondence after initial filing)

Total Number of Pages in This Submission	33

Application Number	10/622,283
Filing Date	July 18, 2003
First Named Inventor	STERN, ROBERT
Group Art Unit	1652
Examiner Name	GEBREYESUS, KAGNEW H.
Attorney Docket Number	UCSF-088CON2

ENCLOSURES (check all that apply)

- ☐ Fee Transmittal Form
  - ☐ Fee Attached
- ☐ Amendment / Reply
  - ☐ After Final
  - ☐ Affidavits/declaration(s)
- ☐ Extension of Time Request
- ☐ Express Abandonment Request
- ☐ Information Disclosure Statement
- ☐ Certified Copy of Priority Documents
- ☐ Response to Missing Parts/ Incomplete Application
  - ☐ Response to Missing Parts under 37 CFR 1.52 or 1.53
- ☐ Assignment Papers *(for an Application)*
- ☐ Drawing(s)
- ☐ Licensing-related Papers
- ☐ Petition
- ☐ Petition to Convert to a Provisional Application
- ☐ Power of Attorney, Revocation Change of Correspondence Address
- ☐ Terminal Disclaimer
- ☐ Request for Refund
- ☐ CD, Number of CD(s
- ☐ After Allowance Communication to Group
- ☐ Appeal Communication to Board of Appeals and Interferences
- ☒ Other Enclosure(s) *(please identify below):*
  1. **Petition for Certificate of Correction (2 pgs.)**
  2. **Certificate of Correction (1 pg.)**
  3. **Copy of Amendment & Response filed 11/17/06 (20 pgs)**
  4. **Examiner Amendment mailed 7/10/06 (7 pgs.)**
  5. **Last 2 pages of issue patent showing changes in red**
  6. **Return Postcard**

Remarks

SIGNATURE OF APPLICANT, ATTORNEY, OR AGENT

Signing Attorney/Agent (Reg. No.)	**EDWARD J. BABA, 52,581** **BOZICEVIC, FIELD & FRANCIS, LLP**
Signature	
Date	**November 7, 2006**

Certificate
NOV 14 2006
of Correction

EXPRESS MAIL LABEL NO. EV 687 640 505 US

Express Mail No. EV 687 640 505 US

PETITION FOR CERTIFICATE OF CORRECTION UNDER 37 C.F.R. § 1.322 FOR PATENT AND TRADEMARK OFFICE ERROR Address to: Mail Stop DAC Commissioner for Patents P.O. Box 1450 Alexandria, VA 22313-1450	Attorney Docket Number	UCSF-088CON2
	First Named Inventor	ROBERT STERN
	Application Number	10/622,283
	Filing Date	July 18, 2003
	Patent Number	7,105,330
	Issue Date	September 12, 2006
	Title	HUMAN PLASMA HYALURONIDASE

Sir:

Applicants petition under 37 C.F.R. § 1.322 for a Certificate of Correction to correct errors in the claims for the above-identified patent due to Patent and Trademark Office error.

Transmitted herewith for filing is a Certificate of Correction for the above-identified patent. Please make the following corrections to Claims 1, 12, 23, and 36.

In Claim 1, column 55, line 42, the word "organicmolecule" should be replaced with -- organic molecule --.

In Claim 1, column 55, line 43, the word "glysolated" should be replaced with -- glycosylated --.

In Claim 1, column 55, line 45, the word -- about -- after the word "above" and before the word "25° C" should be removed.

In Claim 12, column 56, line 42, the word -- polypeptide – should be inserted after the word "hyaluronidase" and before the word "wherein".

In Claim 12, column 56, line 47, the word "iomic" should be replaced with -- ionic --.

In Claim 23, column 57, line 10, the word -- polypeptide – should be inserted after the word "hyaluronidase" and before the word "wherein".

In Claim 36, column 57, line 51, the word -- polypeptide – should be inserted after the word "hyaluronidase" and before the word "wherein".

Enclosed is a copy of the Amendment and Response filed on November 17, 2005, and Examiner's Amendment mailed on July 10, 2006, both showing the correct form of the Claims. Also enclosed, are copies of the last two page of the issued patent showing the incorrect language of the claims that resulted from Patent and Trademark Office error.

It is believed that no fee is due since the error was made by the Patent and Trademark Office. However, the Commissioner is hereby authorized to charge any fees under 37 C.F.R. § 1.20 which may be required by this paper, or to credit any overpayment, to Deposit Account No. 50-0815.

Respectfully submitted,
BOZICEVIC, FIELD & FRANCIS LLP

Date: NOV 7, 2006 By: _____
Edward J. Baba
Registration No. 52,581

BOZICEVIC, FIELD & FRANCIS LLP
1900 University Avenue, Suite 200
East Palo Alto, CA 94303
Telephone: (650) 327-3400
Fax: (650) 327-3231

F:\DOCUMENT\UCSF\088con2\Certificate of Correction Petition UCSF-088CON2.rtf

UNITED STATES PATENT AND TRADEMARK OFFICE
CERTIFICATE OF CORRECTION

PATENT NO. : 7,105,330
DATED : September 12, 2006
INVENTOR(S) : Robert Stern

It is certified that error appears in the above-identified patent and that said Letters Patent are hereby corrected as shown below:

In Claim 1, column 55, line 42, the word "organicmolecule" should be replaced with -- organic molecule --.

In Claim 1, column 55, line 43, the word "glysolated" should be replaced with -- glycosylated --.

In Claim 1, column 55, line 45, the word -- about -- after the word "above" and before the word "25° C" should be removed.

In Claim 12, column 56, line 42, the word -- polypeptide – should be inserted after the word "hyaluronidase" and before the word "wherein".

In Claim 12, column 56, line 47, the word "iomic" should be replaced with -- ionic --.

In Claim 23, column 57, line 10, the word -- polypeptide – should be inserted after the word "hyaluronidase" and before the word "wherein".

In Claim 36, column 57, line 51, the word -- polypeptide – should be inserted after the word "hyaluronidase" and before the word "wherein".

MAILING ADDRESS OF SENDER:

BOZICEVIC, FIELD & FRANCIS LLP
1900 University Avenue, Suite 200
East Palo Alto, CA 94303

PATENT NO: 7,105,330

No. of add'l copies
@ 50¢ per page

NOV 15 2006

COPY

Atty/Sec: PAB/CKH
Atty Docket No. UCSF-088CON2
Date Mailed: November 17, 2005
Application No.: 10/622,283 Filing Date: July 18, 2003

Inventor(s): STERN, ROBERT

Title: "HUMAN PLASMA HYALURONIDASE"

Enclosure(s):

- RCE Transmittal (1 pg.)
- Fee Transmittal (1 pg.)
- Form PTO-2038 (1 pg.)
- Petition for Extension of Time (1 pg.)
- Preliminary Amendment (16 pgs.)
- Exhibits 1-4
- Return Postcard

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Acknowledge Receipt of enclosures
By imprinting PTO Date Stamp and
Returning to addressee

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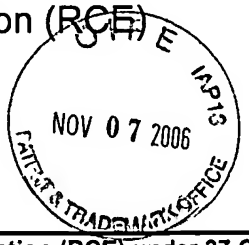
Request For Continued Examination (RCE) Transmittal

Address to:
Mail Stop RCE
Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450



Application Number	10/622,283
Filing Date	July 18, 2003
First Named Inventor	STERN, ROBERT
Art Unit	1652
Examiner Name	GEBREYESUS, KAGNEW
Attorney Docket Number	UCSF-088CON2

This is a Request for Continued Examination (RCE) under 37 C.F.R. § 1.114 of the above-identified application.
Request for Continued Examination (RCE) practice under 37 CFR 1.114 does not apply to any utility or plant application filed prior to June 8, 1995, or to any design application. See Instruction Sheet for RCEs (not to be submitted to the USPTO) on page 2.

1. Submission required under 37 C.F.R. § 1.114 Note: If the RCE is proper, any previously filed unentered amendments and amendments enclosed with the RCE will be entered in the order in which they were filed unless applicant instructs otherwise. If applicant does not wish to have any previously filed unentered amendment(s) entered, applicant must request non-entry of such amendment(s).
   a. ☐ Previously submitted. If a final Office action is outstanding, any amendments filed after the final Office action may be considered as a submission even if this box is not checked.
      ii ☐ Consider the arguments in the Appeal Brief or Rely Brief previously filed on_____
      iii ☐ Other _____
   b. ☒ Enclosed
      i ☐ Amendment/Reply
      ii ☐ Affidavit(s)/Declaration(s)
      iii. ☐ Information Disclosure Statement (IDS)
      iv. ☒ Other **Preliminary Amendment (16 pgs.); Exhibits 1-4**

2. Miscellaneous
   a. ☐ Suspension of action on the above-identified application is requested under 37 C.F.R. § 1.103(c) for a period of _____ months. (Period of suspension shall not exceed 3 months; Fee under 37 C.F.R. § 1.17(l) required)
   b. ☐ Other _____

3. Fees The RCE fee under 37 C.F.R. § 1.17 (e) is required by 37 C.F.R. § 1.114 when RCE is filed.
   a. ☒ The Director is hereby authorized to charge any underpayment or credit any overpayments associated with the following fees to Deposit Account No. **50-0815**.
      i ☒ RCE fee required under 37 C.F.R. § 1.17 (e)
      ii ☒ Extension of time fee (37 C.F.R. §§ 1.136 and 1.17)
      iii ☐ Other _____
   b. ☐ Check in the amount of $ _____ enclosed
   c. ☒ **Payment by credit card** (Form PTO-2038 enclosed)

WARNING: Information on this form may become public. Credit card information should not be included on this form. Provide credit card information and authorization on PTO-2038.

SIGNATURE OF APPLICANT, ATTORNEY, OR AGENT REQUIRED

Signature		Date	November 17, 2005
Name (Print/Type)	Paula A. Borden	Registration No.	42,344

EXPRESS MAIL NO. **EV 687 633 835 US**

This collection of information is required by 37 CFR 1.114. The information is required to obtain or retain a benefit by the public which is to file (and by the USPTO to process) an application. Confidentiality is governed by 35 U.S.C. 122 and 37 CFR 1.14. This collection is estimated to take 12 minutes to complete, including gathering, preparing, and submitting the completed application form to the USPTO. Time will vary depending upon the individual case. Any comments on the amount of time you require to complete this form and/or suggestions for reducing this burden, should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, U.S. Department of Commerce, P.O. Box 1450, Alexandria, VA 22313-1450. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. **SEND TO: Mail Stop RCE, Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.**

If you need assistance in completing the form, call 1-800-PTO-9199 and select option 2.

11/17/05

PTO/SB/17 (12-04)
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Effective on 12/08/2004.
Fees pursuant to the Consolidated Appropriations Act, 2005 (H.R. 4818).

FEE TRANSMITTAL
For FY 2005

☒ Applicant claims small entity status. See 37 CFR 1.27

TOTAL AMOUNT OF PAYMENT ($) 1,605.00

Complete if Known	
Application Number	10/622,283
Filing Date	July 18, 2003
First Named Inventor	STERN, ROBERT
Examiner Name	GEBREYESUS, KAGNEW H.
Art Unit	1652
Attorney Docket No.	UCSF-088CON2

METHOD OF PAYMENT (check all that apply)

☐ Check ☒ **Credit Card** ☐ Money Order ☐ None ☐ Other (please identify): _____

☒ Deposit Account Deposit Account Number: **50-0815** Deposit Account Name: **Bozicevic, Field and Francis LLP**

For the above-identified deposit account, the Director is hereby authorized to: (check all that apply)

☐ Charge fee(s) indicated below ☐ Charge fee(s) indicated below, **except for the filing fee**

☒ Charge any additional fee(s) or underpayments of fee(s) under 37 CFR 1.16 and 1.17 ☒ Credit any overpayments

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FEE CALCULATION

1. BASIC FILING, SEARCH, AND EXAMINATION FEES

	FILING FEES		SEARCH FEES		EXAMINATION FEES		
		Small Entity		Small Entity		Small Entity	
Application Type	Fee ($)	Fee ($)	Fee ($)	Fee ($)	Fee ($)	Fee ($)	Fees Paid ($)
Utility	300	150	500	250	200	100	
Design	200	100	100	50	130	65	
Plant	200	100	300	150	160	80	
Reissue	300	150	500	250	600	300	
Provisional	200	100	0	0	0	0	

2. EXCESS CLAIM FEES

Fee Description	Fee ($)	Small Entity Fee ($)
Each claim over 20 or, for Reissues, each claim over 20 and more than in the original patent	50	25
Each independent claim over 3 or, for Reissues, each independent claim more than in the original patent	200	100
Multiple dependent claims	360	180

Total Claims		Extra Claims	Fee ($)		Fee Paid ($)	Multiple Dependent Claims Fee ($)	Multiple Dependent Claims Fee Paid ($)
80	- 52 or HP =	28	x 25	=	700		

HP = highest number of total claims paid for, if greater than 20

Indep. Claims		Extra Claims	Fee ($)		Fee Paid ($)
6	- 17 or HP =		x	=	

HP = highest number of independent claims paid for, if greater than 3

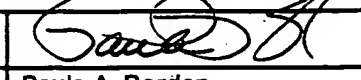
3. APPLICATION SIZE FEE

If the specification and drawings exceed 100 sheets of paper, the application size fee due is $250 ($125 for small entity) for each additional 50 sheets or fraction thereof. See 35 U.S.C. 41(a)(1)(G) and 37 CFR 1.16(s).

Total Sheets		Extra Sheets		Number of each additional 50 or fraction thereof	Fee ($)		Fee Paid ($)
	- 100 =		/ 50 =	(round up to a whole number)	x	=	

4. OTHER FEE(S)

	Fee Paid ($)
Non-English Specification, $130 fee (no small entity discount)	
Other: **RCE Fee and 3-Month Extension of Time**	905.00

SUBMITTED BY			
Signature		Registration No. (Attorney/Agent) 42,344	Telephone (650) 327-3400
Name (Print/Type)	Paula A. Borden		Date 11/17/2005

PTO/SB/22 (12-04)
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U.S. Patent and Trademark Office; U.S. DEPARMENT OF COMMERCE
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PETITION FOR EXTENSION OF TIME UNDER 37 CFR 1.136(a) FY 2005 *(Fees pursuant to the Consolidated Appropriations Act, 2005 (H.R. 4818).)*	Docket Number (Optional) UCSF-088CON2
Application Number: 10/622,283	Filed: July 18, 2003
For: "HUMAN PLASMA HYALURONIDASE"	
Art Unit: 1652	Examiner: GEBREYESUS, KAGNEW H.

This is a request under the provisions of 37 CFR 1.136(a) to extend the period for filing a reply in the above identified application.

The requested extension and fee are as follows (check time period desired and enter the appropriate fee below):

	Fee	Small Entity Fee	
☐ One month (37 CFR 1.17(a)(1))	$120	$60	$_____
☐ Two months (37 CFR 1.17(a)(2))	$450	$225	$_____
☒ Three months (37 CFR 1.17(a)(3))	$1020	$510	$510.00
☐ Four months (37 CFR 1.17(a)(4))	$1590	$795	$_____
☐ Five months (37 CFR 1.17(a)(5))	$2160	$1080	$_____

☐ Applicant claims small entity status. See 37 CFR 1.27.

☐ A check in the amount of the fee is enclosed.

☒ Payment by credit card. Form PTO-2038 is attached.

☐ The Director has already been authorized to charge fees in this application to a Deposit Account.

☒ The Director is hereby authorized to charge any additional fees which may be required, or credit any overpayment, to Deposit Account Number 50-0815.

WARNING: Information on this form may become public. Credit card information should not be included on this form. Provide credit card information and authorization on PTO-2038.

I am the ☐ applicant/inventor

☐ assignee of record of the entire interest. See 37 CFR 3.71. Statement under 37 CFR 3.73(b) is enclosed (Form PTO/SB/96).

☒ attorney or agent of record. Registration Number 42,344

☐ attorney or agent under 37 CFR 1.34.
Registration number if acting under 37 CFR 1.34 _____

Signature

Nov. 17, 2005
Date

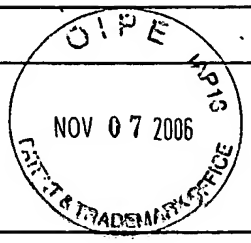
Paula A. Borden
Typed or Printed Name

(650) 327-3400
Telephone Number

NOTE: Signatures of all the inventors or assignees of record of the entire interest or their representative(s) are required. Submit multiple forms if more than one signature is required, see below.

☐ Total of _____ forms are submitted.

This collection of information is required by 37 CFR 1.136(a). The information is required to obtain or retain a benefit by the public which is to file (and by the USPTO to process) an application. Confidentiality is governed by 35 U.S.C. 122 and 37 CFR 1.11 and 1.14. This collection is estimated to take 6 minutes to complete, including gathering, preparing, and submitting the completed application form to the USPTO. Time will vary depending upon the individual case. Any comments on the amount of time you require to complete this form and/or suggestions for reducing this burden, should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, U.S. Department of Commerce, P.O. Box 1450, Alexandria, VA 22313-1450. DO NOT SEND FEES OR COMPLETEDFORMS TO THIS ADDRESS. **SEND TO: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.**
If you need assistance in completing the form, call 1-800-PTO-9199 and select option 2.



Express Mail No. EV 687 633 835 US

PRELIMINARY AMENDMENT	Attorney Docket Confirmation No.	UCSF-088 CON2 4596
	First Named Inventor	R. Stern
	Application Number	10/622,283
	Filing Date	July 18, 2003
Address to: Mail Stop RCE Commissioner for Patents P.O. Box 1450 Alexandria, VA 22313-1450	Group Art Unit	1652
	Examiner Name	K.H. Gebreyesus
	Title	*Human plasma hyaluronidase*

Sir:

This amendment is being filed concurrently with a Request for Continued Examination. This amendment is responsive to the final Office Action dated May 18, 2005 for which a three-month period for response was given, making this response due on or before August 18, 2005. ***A Petition for a three-Month Extension of Time is submitted herewith, making this amendment due on or before November 18, 2005.*** Accordingly, this response is timely filed.

Applicants submit that the amendments set forth below raise no new issues. Rather, the amendments place the claims in form for allowance or in better form for appeal. Entry of these amendments is thus respectfully requested.

In view of the remarks put forth below, reconsideration and allowance are respectfully requested.

I. AMENDMENTS

IN THE CLAIMS

Please enter the amendments to claims 34 and 47, as shown below.

Please enter new claims 87-114, as shown below.

1.-33. (Canceled)

34. (Currently amended) A composition comprising a substantially pure, enzymatically active human plasma hyaluronidase (hpHAse) polypeptide, wherein said polypeptide is glycosylated, and wherein said hpHAse polypeptide partitions into a non-ionic detergent-rich phase at a temperature above about 25°C.

35. (Previously presented) The composition of claim 34, wherein said glycosylated polypeptide is sensitive to N-glycosidase-F treatment.

36. (Previously presented) The composition of claim 34, wherein said glycosylated polypeptide comprises a mannose residue.

37. (Previously presented) The composition of claim 34, wherein said polypeptide further comprises a fatty acid modification.

38. (Previously presented) The composition of claim 37, wherein said fatty acid modification is resistant to phospholipase-C, phospholipase-D, and N-glycosidase-F.

39. (Canceled)

40. (Previously presented) The composition of claim 34, wherein said polypeptide exhibits a specific activity of at least about 6×10^5 relative turbidity reducing units per mg protein.

41. (Previously presented) The composition of claim 34, wherein said polypeptide has a relative molecular mass of about 57 kDa as determined by sodium dodecyl sulfate polyacrylamide gel electrophoresis.

42. (Previously presented) The composition of claim 34, wherein said polypeptide exhibits a specific activity of at least about 2 x 10^5 relative turbidity reducing units per mg protein.

43. (Previously presented) The composition of claim 34, wherein the polypeptide is at least 60% pure.

44. (Previously presented) The composition of claim 34, wherein the polypeptide is at least 75% pure.

45. (Previously presented) The composition of claim 34, wherein the polypeptide is at least 90% pure.

46. (Previously presented) The composition of claim 34, wherein the polypeptide is at least 99% pure.

47. (Currently amended) A composition comprising a recombinant, substantially pure, enzymatically active human plasma hyaluronidase polypeptide, wherein said polypeptide is glycosylated, and wherein said hpHAse polypeptide partitions into a non-ionic detergent-rich phase at a temperature above about 25°C.

48. (Previously presented) The composition of claim 47, wherein said glycosylated polypeptide is sensitive to N-glycosidase-F treatment.

49. (Previously presented) The composition of claim 47, wherein said glycosylated polypeptide comprises a mannose residue.

50. (Previously presented) The composition of claim 47, wherein said polypeptide further comprises a fatty acid modification.

51. (Previously presented) The composition of claim 50, wherein said fatty acid modification is resistant to phospholipase-C, phospholipase-D, and N-glycosidase-F.

52. (Previously presented) The composition of claim 47, wherein said polypeptide exhibits a specific activity of at least about 2×10^5 relative turbidity reducing units per mg protein.

53. (Previously presented) The composition of claim 47, wherein said polypeptide exhibits a specific activity of at least about 6×10^5 relative turbidity reducing units per mg protein.

54. (Previously presented) The composition of claim 47, wherein said polypeptide has a relative molecular mass of about 57 kDa as determined by sodium dodecyl sulfate polyacrylamide gel electrophoresis.

55. (Previously presented) The composition of claim 47, wherein the polypeptide is at least 60% pure.

56. (Previously presented) The composition of claim 47, wherein the polypeptide is at least 75% pure.

57. (Previously presented) The composition of claim 47, wherein the polypeptide is at least 90% pure.

58. (Previously presented) The composition of claim 47, wherein the polypeptide is at least 99% pure.

59. (Previously presented) A formulation comprising

a) a therapeutically effective amount of a substantially pure, enzymatically active human plasma hyaluronidase polypeptide, wherein said polypeptide is glycosylated; and

b) a pharmaceutically acceptable carrier.

60. (Previously presented) The formulation of claim 59, wherein the carrier is a liposome.

61. (Previously presented) The formulation of claim 59, wherein said polypeptide exhibits a specific activity of at least about 2 x 10^5 relative turbidity reducing units per mg protein.

62. (Previously presented) The formulation of claim 59, wherein the human plasma hyaluronidase polypeptide is present at a concentration of about 1.5 x 10^5 turbidity reducing units per milliliter of formulation.

63. (Previously presented) The formulation of claim 59, wherein said glycosylated polypeptide is sensitive to N-glycosidase-F treatment.

64. (Previously presented) The formulation of claim 59, wherein said glycosylated polypeptide comprises a mannose residue.

65. (Previously presented) The formulation of claim 59, wherein said polypeptide further comprises a fatty acid modification.

66. (Previously presented) The formulation of claim 65, wherein said fatty acid modification is resistant to phospholipase-C, phospholipase-D, and N-glycosidase-F.

67. (Previously presented) The formulation of claim 59, wherein said polypeptide exhibits a specific activity of at least about 6 x 10^5 relative turbidity reducing units per mg protein.

68. (Previously presented) The formulation of claim 59, wherein said polypeptide has a relative molecular mass of about 57 kDa as determined by sodium dodecyl sulfate polyacrylamide gel electrophoresis.

69. (Previously presented) The formulation of claim 59, wherein the polypeptide is at least 60% pure.

70. (Previously presented) The formulation of claim 59, wherein the polypeptide is at least 75% pure.

71. (Previously presented) The formulation of claim 59, wherein the polypeptide is at least 90% pure.

72. (Previously presented) The formulation of claim 59, wherein the polypeptide is at least 99% pure.

73. (Previously presented) A formulation comprising

a) a therapeutically effective amount of a recombinant, substantially pure, enzymatically active human plasma hyaluronidase polypeptide, wherein said polypeptide is glycosylated; and

b) a pharmaceutically acceptable carrier.

74. (Previously presented) The formulation of claim 73, wherein the carrier is a liposome.

75. (Previously presented) The formulation of claim 73, wherein said polypeptide exhibits a specific activity of at least about 2×10^5 relative turbidity reducing units per mg protein.

76. (Previously presented) The formulation of claim 73, wherein the human plasma hyaluronidase polypeptide is present at a concentration of about 1.5×10^5 turbidity reducing units per milliliter of formulation.

77. (Previously presented) The formulation of claim 73, wherein said glycosylated polypeptide is sensitive to N-glycosidase-F treatment.

78. (Previously presented) The formulation of claim 73, wherein said glycosylated polypeptide comprises a mannose residue.

79. (Previously presented) The formulation of claim 73, wherein said polypeptide further comprises a fatty acid modification.

80. (Previously presented) The formulation of claim 79, wherein said fatty acid modification is resistant to phospholipase-C, phospholipase-D, and N-glycosidase-F.

81. (Previously presented) The formulation of claim 73, wherein said polypeptide exhibits a specific activity of at least about 6×10^5 relative turbidity reducing units per mg protein.

82. (Previously presented) The formulation of claim 73, wherein said polypeptide has a relative molecular mass of about 57 kDa as determined by sodium dodecyl sulfate polyacrylamide gel electrophoresis.

83. (Previously presented) The formulation of claim 73, wherein the polypeptide is at least 60% pure.

84. (Previously presented) The formulation of claim 73, wherein the polypeptide is at least 75% pure.

85. (Previously presented) The formulation of claim 73, wherein the polypeptide is at least 90% pure.

86. (Previously presented) The formulation of claim 73, wherein the polypeptide is at least 99% pure.

87. (New) A composition comprising a substantially pure, enzymatically active human plasma hyaluronidase (hpHAse) polypeptide, wherein said polypeptide is glycosylated, and wherein said hpHAse polypeptide exhibits β-1,4-endoglycosidase activity and a pH optimum below about pH 4.5.

88. (New) The composition of claim 87, wherein the hpHAse polypeptide exhibits a pH optimum of between about pH 3.0 and about pH 4.0.

89. (New) The composition of claim 87, wherein the hpHAse polypeptide exhibits a pH optimum of between about pH 3.0 and about pH 3.7.

90. (New) The composition of claim 87, wherein said glycosylated polypeptide is sensitive to N-glycosidase-F treatment.

91. (New) The composition of claim 87, wherein said glycosylated polypeptide comprises a mannose residue.

92. (New) The composition of claim 87, wherein said polypeptide further comprises a fatty acid modification.

93. (New) The composition of claim 92, wherein said fatty acid modification is resistant to phospholipase-C, phospholipase-D, and N-glycosidase-F.

94. (New) The composition of claim 87, wherein said polypeptide exhibits a specific activity of at least about 6×10^5 relative turbidity reducing units per mg protein.

95. (New) The composition of claim 87, wherein said polypeptide has a relative molecular mass of about 57 kDa as determined by sodium dodecyl sulfate polyacrylamide gel electrophoresis.

96. (Previously presented) The composition of claim 87, wherein said polypeptide exhibits a specific activity of at least about 2×10^5 relative turbidity reducing units per mg protein.

97. (New) The composition of claim 87, wherein the polypeptide is at least 60% pure.

98. (New) The composition of claim 87, wherein the polypeptide is at least 75% pure.

99. (New) The composition of claim 87, wherein the polypeptide is at least 90% pure.

100. (New) The composition of claim 87, wherein the polypeptide is at least 99% pure.

101. (New) A composition comprising a recombinant, substantially pure, enzymatically active human plasma hyaluronidase (hpHAse) polypeptide, wherein said polypeptide is glycosylated, and wherein said hpHAse polypeptide exhibits β-1,4-endoglycosidase activity and a pH optimum below about pH 4.5.

102. (New) The composition of claim 101, wherein the hpHAse polypeptide exhibits a pH optimum of between about pH 3.0 and about pH 4.0.

103. (New) The composition of claim 101, wherein the hpHAse polypeptide exhibits a pH optimum of between about pH 3.0 and about pH 3.7.

104. (New) The composition of claim 101, wherein said glycosylated polypeptide is sensitive to N-glycosidase-F treatment.

105. (New) The composition of claim 101, wherein said glycosylated polypeptide comprises a mannose residue.

106. (New) The composition of claim 101, wherein said polypeptide further comprises a fatty acid modification.

107. (New) The composition of claim 106, wherein said fatty acid modification is resistant to phospholipase-C, phospholipase-D, and N-glycosidase-F.

108. (New) The composition of claim 101, wherein said polypeptide exhibits a specific activity of at least about 2×10^5 relative turbidity reducing units per mg protein.

109. (New) The composition of claim 101, wherein said polypeptide exhibits a specific activity of at least about 6×10^5 relative turbidity reducing units per mg protein.

110. (New) The composition of claim 101, wherein said polypeptide has a relative molecular mass of about 57 kDa as determined by sodium dodecyl sulfate polyacrylamide gel electrophoresis.

111. (New) The composition of claim 101, wherein the polypeptide is at least 60% pure.

112. (New) The composition of claim 101, wherein the polypeptide is at least 75% pure.

113. (New) The composition of claim 101, wherein the polypeptide is at least 90% pure.

114. (New) The composition of claim 101, wherein the polypeptide is at least 99% pure.

II. REMARKS

Formal Matters

Claims 34-38 and 40-114are pending after entry of the amendments set forth herein.

Claims 34-38 and 40-86 were examined and were rejected.

Claims 34 and 47 are amended. The amendments to the claims were made solely in the interest of expediting prosecution, and are not to be construed as acquiescence to any objection or rejection of any claim. Support for the amendments to claims 34 and 47 is found in the claims as originally filed, and throughout the specification, in particular at the following locations: page 13, lines 10-11; page 22, lines 14-16; page 23, lines 3-5; and Example 2, page 52, line 22 to page 53, line 11. Accordingly, no new matter is added by these amendments.

Claims 87-114 are added. Support for new claims 87-114 is found in the claims as originally filed, and throughout the specification, including the following exemplary locations: claims 87, 88, 101, and 102: page 13, lines 2-5; page 21, lines 13-16; Example 11, page 66, line 22 to page 67, line 10; and Figure 8; claims 89 and 103: page 21, lines 13-16; claims 90 and 104: page 54, lines 23-24; claims 91 and 105: page 55, lines 20-21; claims 92 and 106: page 13, line 11; claims 93 and 107: page 8, lines 15-19; claims 94, 96, 108, and 109: page 13, lines 7-8, and page 54, Table 1; claims 95 and 110: page 13, lines 5-7; and claims 96-100, and 110-114: page 15, lines 1-10. Accordingly, no new matter is added by these new claims.

Applicants respectfully request reconsideration of the application in view of the remarks made herein.

Rejection under 35 U.S.C.§112, first paragraph

Claims 34, 36, 37, 43-47, 49, 50, and 54-58 were rejected under 35 U.S.C.§112, first paragraph, as allegedly failing to comply with the written description requirement.

The Office Action stated that the claims are directed to a genus of DNA molecules encoding any hyaluronidase polypeptide from plasma. The Office Action stated that the specification teaches only a partial structure of a single representative species of a plasma hyaluronidase polypeptide; and that the specification fails to describe any other representative species by any identifying characteristics or properties other than the functionality of hyaluronidase polypeptide. Applicants respectfully traverse the rejection.

The Office Action stated that the specification teaches only a partial structure of a single representative species of a plasma hyaluronidase polypeptide. However, as the Office Action acknowledged, the specification teaches two plasma hyaluronidase amino acid sequences: SEQ ID NOs:1 and 3.

The Office Action stated that the claims encompass not only the two plasma hyaluronidases described in the specification, but also any enzyme with or without hyaluronidase activity from any source. However, the claims recite that the plasma hyaluronidase polypeptide is "enzymatically active." As such, the claim language excludes plasma hyaluronidase polypeptides that are not enzymatically active.

The Office Action stated that the claimed hpHases encompass hpHAse with substitutions, deletions, and additions, as defined in the specification; and that this definition renders the claims beyond the scope of what has been described, since hyaluronidases other than plasma hyaluronidases that exhibit hyaluronidase activity are also encompassed by this definition. However, the instant specification provides ample description of human plasma hyaluronidase (hpHAse) polypeptides; and describes a number of identifying features of the enzyme. Specification, page 13, line 2 to page 14, line 4. The specification states that the term hpHAse encompasses polypeptides having amino acid sequences that are modified relative to a naturally-occurring amino acid sequence of hpHase due to amino acid substitution, deletion, and/or addition. Specification, page 13, line 25 to page 14, line 1. Furthermore, as noted above, the specification provides **two** amino acid sequences of hpHAse polypeptides. Specification, page 13, lines 15-25; page 33, lines 9-11; page 33, lines 23-29; and SEQ ID NOs:1 and 3.

Applicants submit that, given 1) the disclosure of two hpHAse polypeptide amino acid sequences; 2) the high skill level of those in the art with respect to identifying variants of polypeptides; and 3) the disclosure in the specification of several identifying features of hpHAse polypeptides, those skilled in the art would reasonably conclude that the Applicants had possession of the claimed invention.

Nevertheless, and solely in the interest of expediting prosecution, claims 34 and 47 are amended to recite that the hpHAse polypeptide partitions into a non-ionic detergent-rich phase at a temperature above about 25°C.

Conclusion as to the rejection under 35 U.S.C.§112, first paragraph

Applicants submit that the rejection of claims 34, 36, 37, 43-47, 49, 50, and 54-58 under 35 U.S.C. §112, first paragraph, has been adequately addressed in view of the remarks set forth above. The Examiner is thus respectfully requested to withdraw the rejection.

Rejection under 35 U.S.C.§102(b)

Claims 34-38 and 40-58 were rejected under 35 U.S.C.§102(b) as allegedly anticipated by Affify et al. ((1993) *Arch. Biochem. Biophys.* 305:434-441; "Afify").

The Office Action stated that Afify discloses the purification of a hyaluronidase from fresh human serum to apparent homogeneity. The Office Action stated that Afify's enzyme is active and purified to apparent homogeneity. Applicants respectfully traverse the rejection.

Purification of hpHAse

The instant invention relates to highly purified hpHAse. The hpHAse is purified to a degree not previously disclosed. The material discussed in Afify is a crude preparation, and as such contains plasma protein contaminants. Indeed, Afify indicates that the hpHAse composition discussed therein exhibited a specific activity of only 53.3 units per mg protein. Afify, page 438, Table 1. Afify does not disclose a composition comprising a hpHAse that is purified to a degree disclosed in the instant application, where the hpHAse is substantially pure. Accordingly, Afify cannot anticipate the instant invention as claimed.

Furthermore, as discussed in the accompanying Declaration of Robert Stern, provide herewith as Exhibit 1, human serum hyaluronidase was not purified to apparent homogeneity, as asserted by Afify; instead, human serum hyaluronidase represented less than 1% of the total protein in the preparation identified by Afify as purified human serum hyaluronidase. This is because human plasma hyaluronidase is present in human serum at concentrations that are too low to give rise to the amount of serum hyaluronidase asserted by Afify from only 1.2 ml serum. Indeed, the protein that is shown in Figure 3B of Afify, and identified in the legend of Figure 3B as "purified human serum hyaluronidase, proved upon amino acid sequence of the N-terminus of protein extracted from the band to be human serum albumin. That the protein preparation asserted by Afify to be purified human serum

hyaluronidase consisted primarily of human serum albumin is not surprising, in view of the abundance of albumin in human serum.

Specific activity

The Office Action stated that claims 40, 42, 52, and 53 are rejected, because the units used to define specific activity of the hyaluronidase in Afify differs from the units used to define specific activity in the instant application; and that Applicants have not provided a Declaration regarding the relationship between the units.

As discussed in the accompanying Declaration of Robert Stern, Afify used a different method to determine enzyme activity from the method described in the instant application. Afify used a method referred to in the Declaration as the "Stern and Stern" method, while the method used in the instant application is referred to as the "Frost and Stern" method. As explained in the Declaration of Robert Stern, there are approximately 6 (Stern and Stern) Units for every (Frost and Stern) Unit. However, conversion is not required to evaluate the purity of the preparations described by Afify and those described in the instant application. As discussed above, and in the Declaration of Robert Stern, human serum hyaluronidase was not purified to apparent homogeneity, as asserted by Afify; instead, human serum hyaluronidase represented less than 1% of the total protein in the preparation identified by Afify as purified human serum hyaluronidase. Accordingly, Afify cannot anticipate claims 34-38 and 40-58.

Conclusion as to the rejection under 35 U.S.C.§102(b)

In view of the facts presented above, Afify does not disclose or suggest a composition comprising substantially pure, enzymatically active hpHAse, as claimed. Accordingly, Afify cannot anticipate claims 34-38 and 40-58.

Applicants submit that the rejection of claims 34-38 and 40-58 under 35 U.S.C. §102(b) has been adequately addressed in view of the remarks set forth above. The Examiner is thus respectfully requested to withdraw the rejection.

Rejection under 35 U.S.C.§103(a)

Claims 59-86 were rejected under 35 U.S.C.§103(a) as allegedly unpatentable over Baumgartner et al. ((1988) *Reg. Cancer Treat.* 1:55-58; "Baumgartner") in view of Afify.

The Office Action stated that Baumgartner teaches the use of a hyaluronidase composition in a Phase I trial in chemoresistant loco-regional malignant disease. The Office Action stated that one of

ordinary skill in the art would be motivated to use the purified hyaluronidase of Afify for the treatment of malignant disease such s the disease disclosed by Baumgartner. The Office Action concluded that it would have been obvious to prepare a composition of the protein of Afify together with a pharmaceutical carrier. Applicants respectfully traverse the rejection.

Baumgartner discusses use of **bull testis hyaluronidase,** not human plasma hyaluronidase. Bull testis hyaluronidase and human plasma hyaluronidase have different molecular, immunologic and biochemical properties. Baumgartner states that the bull testis hyaluronidase used was highly purified. Baumgartner, page 55, column 2, second paragraph under "Materials and Methods." There is no mention in Baumgartner of human plasma hyaluronidase, much less a pharmaceutical formulation comprising human plasma hyaluronidase. There is no motivation in Baumgartner to prepare a formulation comprising substantially pure human plasma hyaluronidase and a pharmaceutically acceptable carrier.

Afify does not cure the deficiency of Baumgartner. As discussed above, Afify does not disclose a composition comprising substantially pure, enzymatically active hpHAse. Accordingly, Baumgartner, alone or in combination with Afify, cannot render claims 59-86 obvious.

Applicants submit that the rejection of claims 59-86 under 35 U.S.C. §103(a) has been adequately addressed in view of the remarks set forth above. The Examiner is thus respectfully requested to withdraw the rejection.

III. CONCLUSION

Applicants submit that all of the claims are in condition for allowance, which action is requested. If the Examiner finds that a telephone conference would expedite the prosecution of this application, the Examiner is invited to telephone the undersigned at the number provided.

The Commissioner is hereby authorized to charge any underpayment of fees associated with this communication, including any necessary fees for extensions of time, or credit any overpayment to Deposit Account No. 50-0815, order number UCSF-088 CON2.

Respectfully submitted,
BOZICEVIC, FIELD & FRANCIS LLP

Date: Nov. 17, 2005

By: _____
Paula A. Borden
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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/622,283	07/18/2003	Robert Stern	UCSF-088CON2	4596

24353 7590 07/10/2006

BOZICEVIC, FIELD & FRANCIS LLP
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SUITE 200
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EXAMINER	
GEBREYESUS, KAGNEW H	
ART UNIT	PAPER NUMBER
1652	

DATE MAILED: 07/10/2006

COPY

Please find below and/or attached an Office communication concerning this application or proceeding.

KH
7/13

PAB

07/14/06
DOCKETED
Interview Summary 08/10/06

Supplemental Notice of Allowability	Application No. 10/622,283	Applicant(s) STERN ET AL	
	Examiner Kagnew H. Gebreyesus	Art Unit 1652	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address--

All claims being allowable, PROSECUTION ON THE MERITS IS (OR REMAINS) CLOSED in this application. If not included herewith (or previously mailed), a Notice of Allowance (PTOL-85) or other appropriate communication will be mailed in due course. **THIS NOTICE OF ALLOWABILITY IS NOT A GRANT OF PATENT RIGHTS.** This application is subject to withdrawal from issue at the initiative of the Office or upon petition by the applicant. See 37 CFR 1.313 and MPEP 1308.

1. ☒ This communication is responsive to *11/17/05*.

2. ☒ The allowed claim(s) is/are *34-38, 40-42, 44-54, 56-68, 70-82, 84-96, 98-110, 112-114 with amendments*.

3. ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
   a) ☐ All b) ☐ Some* c) ☐ None of the:
      1. ☐ Certified copies of the priority documents have been received.
      2. ☐ Certified copies of the priority documents have been received in Application No. _____ .
      3. ☐ Copies of the certified copies of the priority documents have been received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

   * Certified copies not received: _____.

Applicant has THREE MONTHS FROM THE "MAILING DATE" of this communication to file a reply complying with the requirements noted below. Failure to timely comply will result in ABANDONMENT of this application.
THIS THREE-MONTH PERIOD IS NOT EXTENDABLE.

4. ☐ A SUBSTITUTE OATH OR DECLARATION must be submitted. Note the attached EXAMINER'S AMENDMENT or NOTICE OF INFORMAL PATENT APPLICATION (PTO-152) which gives reason(s) why the oath or declaration is deficient.

5. ☐ CORRECTED DRAWINGS (as "replacement sheets") must be submitted.
   (a) ☐ including changes required by the Notice of Draftsperson's Patent Drawing Review (PTO-948) attached
      1) ☐ hereto or 2) ☐ to Paper No./Mail Date _____.
   (b) ☐ including changes required by the attached Examiner's Amendment / Comment or in the Office action of Paper No./Mail Date _____.

   Identifying indicia such as the application number (see 37 CFR 1.84(c)) should be written on the drawings in the front (not the back) of each sheet. Replacement sheet(s) should be labeled as such in the header according to 37 CFR 1.121(d).

6. ☐ DEPOSIT OF and/or INFORMATION about the deposit of BIOLOGICAL MATERIAL must be submitted. Note the attached Examiner's comment regarding REQUIREMENT FOR THE DEPOSIT OF BIOLOGICAL MATERIAL.

Attachment(s)

1. ☐ Notice of References Cited (PTO-892)
2. ☐ Notice of Draftperson's Patent Drawing Review (PTO-948)
3. ☐ Information Disclosure Statements (PTO-1449 or PTO/SB/08), Paper No./Mail Date _____
4. ☐ Examiner's Comment Regarding Requirement for Deposit of Biological Material
5. ☐ Notice of Informal Patent Application (PTO-152)
6. ☒ Interview Summary (PTO-413), Paper No./Mail Date *12/08/2005*.
7. ☐ Examiner's Amendment/Comment
8. ☒ Examiner's Statement of Reasons for Allowance
9. ☐ Other _____.

DETAILED ACTION

EXAMINER'S AMENDMENT

1. An examiner's amendment to the record appears below. Should the changes and/or additions be unacceptable to applicant, an amendment may be filed as provided by 37 CFR 1.312. To ensure consideration of such an amendment, it MUST be submitted no later than the payment of the issue fee.

Authorization for this examiner's amendment was given in a telephone interview with Attorney Paula Borden on December 8, 2005.

1. The following is an examiner's statement of reasons for allowance:

In claim 34, 47, 59, 73, 87, 101:

Replace: "...human plasma hyaluronidase..." with ***"...naturally occurring human plasma hyaluronidase..."***

Replace: "...wherein said polypeptide is glycosylated,..." with

"...wherein said polypeptide is at least 60%, by weight, free from the proteins and naturally-occurring organic molecules with which it is naturally associated and wherein said polypeptide is glycosylated,..."

In claims 40, 42, 52, 53, 61, 67, 75, 81, 94, 96, 108 and 109 replace:

- at least about -- with -- ***at least***--.

In claim 47 replace:

- above about -- with -- ***above*** --

In claim 87, 101 replace:

- "... below about..." with "... below..."

Canceled claims:

43, 55, 69, 83, 97 and 111 are cancelled given that these claims are encompassed in the limitation of the independent claims.

Reason for allowance:

The claims directed to a substantially purified preparation of naturally occurring biologically active human plasma hyaluronidase enzymes as disclosed on page 13 line 2-24. Applicant's submission of a declaration under 1.132 and the clarification provided contrasting their plasma hyaluronidase preparation and Affify's plasma hyaluronidase purification in terms of the steps, starting material and most importantly the activity/unit enzyme is persuasive. In addition although the prior art (Bader et al.) teaches a Human tumor suppressor (LUCA-1) mRNA and deduced amino acid sequence identical to the human plasma hyaluronidase identified by applicants, the disclosure does not teach a human plasma hyaluronidase enzyme or a recombinant human plasma hyaluronidase enzyme substantially purified $6x10^5$ rTRU as shown by the applicants. Therefore the claims drawn to a substantially pure naturally occurring human plasma hyaluronidase enzyme is allowed.

Any comments considered necessary by applicant must be submitted no later than the payment of the issue fee and, to avoid processing delays, should preferably accompany the issue

fee. Such submissions should be clearly labeled "Comments on Statement of Reasons for Allowance."

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Kagnew H. Gebreyesus whose telephone number is 571-272-2937. The examiner can normally be reached on 8:30 am - 5: 30 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Achutamurthy ponnathapura can be reached on 571-272-0928. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Kagnew Gebreyesus PhD.

REBECCA E. PRUTY
PRIMARY EXAMINER
GROUP 1600

Interview Summary	Application No.	Applicant(s)	
	10/622,283	STERN ET AL.	
	Examiner	Art Unit	
	Kagnew H. Gebreyesus	1652	

All participants (applicant, applicant's representative, PTO personnel):

(1) *Kagnew H. Gebreyesus*. (3)_____.

(2) *Attorney Paula Borden*. (4)_____.

Date of Interview: *08 December 2005*.

Type: a)☒ Telephonic b)☐ Video Conference
c)☐ Personal [copy given to: 1)☐ applicant 2)☐ applicant's representative]

Exhibit shown or demonstration conducted: d)☐ Yes e)☐ No.
If Yes, brief description: _____.

Claim(s) discussed: *34-38 and 40-42, 44-54, 56-68, 70-82, 84-96, 98-110, 112-114*.

Identification of prior art discussed: _____.

Agreement with respect to the claims f)☒ was reached. g)☐ was not reached. h)☐ N/A.

Substance of Interview including description of the general nature of what was agreed to if an agreement was reached, or any other comments: *Claim amendments proposed by examiner was accepted.*.

(A fuller description, if necessary, and a copy of the amendments which the examiner agreed would render the claims allowable, if available, must be attached. Also, where no copy of the amendments that would render the claims allowable is available, a summary thereof must be attached.)

THE FORMAL WRITTEN REPLY TO THE LAST OFFICE ACTION MUST INCLUDE THE SUBSTANCE OF THE INTERVIEW. (See MPEP Section 713.04). If a reply to the last Office action has already been filed, APPLICANT IS GIVEN A NON-EXTENDABLE PERIOD OF THE LONGER OF ONE MONTH OR THIRTY DAYS FROM THIS INTERVIEW DATE, OR THE MAILING DATE OF THIS INTERVIEW SUMMARY FORM, WHICHEVER IS LATER, TO FILE A STATEMENT OF THE SUBSTANCE OF THE INTERVIEW. See Summary of Record of Interview requirements on reverse side or on attached sheet.

Examiner Note: You must sign this form unless it is an Attachment to a signed Office action.

Kagnew G. Yesus
Examiner's signature, if required

Summary of Record of Interview Requirements

Manual of Patent Examining Procedure (MPEP), Section 713.04, Substance of Interview Must be Made of Record
A complete written statement as to the substance of any face-to-face, video conference, or telephone interview with regard to an application must be made of record in the application whether or not an agreement with the examiner was reached at the interview.

Title 37 Code of Federal Regulations (CFR) § 1.133 Interviews
Paragraph (b)
In every instance where reconsideration is requested in view of an interview with an examiner, a complete written statement of the reasons presented at the interview as warranting favorable action must be filed by the applicant. An interview does not remove the necessity for reply to Office action as specified in §§ 1.111, 1.135. (35 U.S.C. 132)

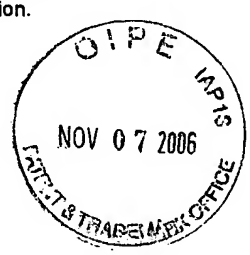
37 CFR §1.2 Business to be transacted in writing.
All business with the Patent or Trademark Office should be transacted in writing. The personal attendance of applicants or their attorneys or agents at the Patent and Trademark Office is unnecessary. The action of the Patent and Trademark Office will be based exclusively on the written record in the Office. No attention will be paid to any alleged oral promise, stipulation, or understanding in relation to which there is disagreement or doubt.

The action of the Patent and Trademark Office cannot be based exclusively on the written record in the Office if that record is itself incomplete through the failure to record the substance of interviews.

It is the responsibility of the applicant or the attorney or agent to make the substance of an interview of record in the application file, unless the examiner indicates he or she will do so. It is the examiner's responsibility to see that such a record is made and to correct material inaccuracies which bear directly on the question of patentability.

Examiners must complete an Interview Summary Form for each interview held where a matter of substance has been discussed during the interview by checking the appropriate boxes and filling in the blanks. Discussions regarding only procedural matters, directed solely to restriction requirements for which interview recordation is otherwise provided for in Section 812.01 of the Manual of Patent Examining Procedure, or pointing out typographical errors or unreadable script in Office actions or the like, are excluded from the interview recordation procedures below. Where the substance of an interview is completely recorded in an Examiners Amendment, no separate Interview Summary Record is required.

The Interview Summary Form shall be given an appropriate Paper No., placed in the right hand portion of the file, and listed on the "Contents" section of the file wrapper. In a personal interview, a duplicate of the Form is given to the applicant (or attorney or agent) at the conclusion of the interview. In the case of a telephone or video-conference interview, the copy is mailed to the applicant's correspondence address either with or prior to the next official communication. If additional correspondence from the examiner is not likely before an allowance or if other circumstances dictate, the Form should be mailed promptly after the interview rather than with the next official communication.



The Form provides for recordation of the following information:
- Application Number (Series Code and Serial Number)
- Name of applicant
- Name of examiner
- Date of interview
- Type of interview (telephonic, video-conference, or personal)
- Name of participant(s) (applicant, attorney or agent, examiner, other PTO personnel, etc.)
- An indication whether or not an exhibit was shown or a demonstration conducted
- An identification of the specific prior art discussed
- An indication whether an agreement was reached and if so, a description of the general nature of the agreement (may be by attachment of a copy of amendments or claims agreed as being allowable). Note: Agreement as to allowability is tentative and does not restrict further action by the examiner to the contrary.
- The signature of the examiner who conducted the interview (if Form is not an attachment to a signed Office action)

It is desirable that the examiner orally remind the applicant of his or her obligation to record the substance of the interview of each case. It should be noted, however, that the Interview Summary Form will not normally be considered a complete and proper recordation of the interview unless it includes, or is supplemented by the applicant or the examiner to include, all of the applicable items required below concerning the substance of the interview.

A complete and proper recordation of the substance of any interview should include at least the following applicable items:
1) A brief description of the nature of any exhibit shown or any demonstration conducted,
2) an identification of the claims discussed,
3) an identification of the specific prior art discussed,
4) an identification of the principal proposed amendments of a substantive nature discussed, unless these are already described on the Interview Summary Form completed by the Examiner,
5) a brief identification of the general thrust of the principal arguments presented to the examiner,
   (The identification of arguments need not be lengthy or elaborate. A verbatim or highly detailed description of the arguments is not required. The identification of the arguments is sufficient if the general nature or thrust of the principal arguments made to the examiner can be understood in the context of the application file. Of course, the applicant may desire to emphasize and fully describe those arguments which he or she feels were or might be persuasive to the examiner.)
6) a general indication of any other pertinent matters discussed, and
7) if appropriate, the general results or outcome of the interview unless already described in the Interview Summary Form completed by the examiner.

Examiners are expected to carefully review the applicant's record of the substance of an interview. If the record is not complete and accurate, the examiner will give the applicant an extendable one month time period to correct the record.

Examiner to Check for Accuracy

If the claims are allowable for other reasons of record, the examiner should send a letter setting forth the examiner's version of the statement attributed to him or her. If the record is complete and accurate, the examiner should place the indication, "Interview Record OK" on the paper recording the substance of the interview along with the date and the examiner's initials.

-continued

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Arg Ile Val Phe Thr Asp Gln Val Leu Lys Phe Leu Ser Gln Asp Glu
305                 310                 315                 320

Leu Val Tyr Thr Phe Gly Glu Thr Val Ala Leu Gly Ala Ser Gly Ile
                325                 330                 335

Val Ile Trp Gly Thr Leu Ser Ile Met Arg Ser Met Lys Ser Cys Leu
            340                 345                 350

Leu Leu Asp Asn Tyr Met Glu Thr Ile Leu Asn Pro Tyr Ile Ile Asn
        355                 360                 365

Val Thr Leu Ala Ala Lys Met Cys Ser Gln Val Leu Cys Gln Glu Gln
    370                 375                 380

Gly Val Cys Ile Arg Lys Asn Trp Asn Ser Ser Asp Tyr Leu His Leu
385                 390                 395                 400

Asn Pro Asp Asn Phe Ala Ile Gln Leu Glu Lys Gly Gly Lys Phe Thr
                405                 410                 415

Val Arg Gly Lys Pro Thr Leu Glu Asp Leu Glu Gln Phe Ser Glu Lys
            420                 425                 430

Phe Tyr Cys Ser Cys Tyr Ser Thr Leu Ser Cys Lys Glu Lys Ala Asp
        435                 440                 445

Val Lys Asp Thr Asp Ala Val Asp Val Cys Ile Ala Asp Gly Val Cys
    450                 455                 460

Ile Asp Ala Phe Leu Lys Pro Pro Met Glu Thr Glu Glu Pro Gln Ile
465                 470                 475                 480

Phe Tyr Asn Ala Ser Pro Ser Thr Leu Ser Ala Thr Met Phe Ile Val
                485                 490                 495

Ser Ile Leu Phe Leu Ile Ile Ser Ser Val Ala Ser Leu
            500                 505
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What is claimed is:

1. A composition comprising a substantially pure, enzymatically active naturally occuring human plasma hyaluronidase (hpHAse) polypeptide, wherein said polypeptide is at least 60%, by weight, free from the proteins and naturally-occurring organicmolecules with which it is naturally associated and wherein said polypeptide is glysolated, and wherein said hpHAse polypeptide partitions into a non-ionic detergent-rich phase at a temperature above about 25° C.

2. The composition of claim 1, wherein said glycosylated polypeptide is sensitive to N-glycosidase-F treatment.

3. The composition of claim 1, wherein said glycosylated polypeptide comprises a mannose residue.

4. The composition of claim 1, wherein said polypeptide further comprises a fatty acid modification.

5. The composition of claim 4, wherein said fatty acid modification is resistant to phospholipase-C, phospholipase-D, and N-glycosidase-F.

6. The composition of claim 1, wherein said polypeptide exhibits a specific activity of at least 6×10^5 relative turbidity reducing units per mg protein.

7. The composition of claim 1, wherein said polypeptide has a relative molecular mass of about 57 kDa as determined by sodium dodecyl sulfate polyacrylamide gel electrophoresis.

8. The composition of claim 1, wherein said polypeptide exhibits a specific activity of at least 2×10^5 relative turbidity reducing units per mg protein.

9. The composition of claim 1, wherein the polypeptide is at least 75% pure.

10. The composition of claim 1, wherein the polypeptide is at least 90% pure.

11. The composition of claim 1, wherein the polypeptide is at least 99% pure.

12. A composition comprising a recombinant, substantially pure, naturally occuring human plasma hyaluronidase, wherein said polypeptide is at least 60%, by weight, free from the proteins and naturally-occurring organic molecules with which it is naturally associated and wherein said polypeptide is glycosylated, and wherein said hpHAse polypeptide partitions into a non-ionic detergent-rich phase at a temperature above 25° C.

13. The composition of claim 12, wherein said glycosylated polypeptide is sensitive to N-glycosidase-F treatment.

14. The composition of claim 12, wherein said glycosylated polypeptide comprises a mannose residue.

15. The composition of claim 12, wherein said polypeptide further comprises a fatty acid modification.

16. The composition of claim 15, wherein said fatty acid modification is resistant to phospholipase-C, phospholipase-D, and N-glycosidase-F.

17. The composition of claim 12, wherein said polypeptide exhibits a specific activity of at least about 2×10^5 relative turbidity reducing units per mg protein.

18. The composition of claim 12, wherein said polypeptide exhibits a specific activity of at least about 6×10^5 relative turbidity reducing units per mg protein.

19. The composition of claim 12, wherein said polypeptide has a relative molecular mass of about 57 kDa as determined by sodium dodecyl sulfate polyacrylamide gel electrophoresis.

20. The composition of claim 12, wherein the polypeptide is at least 75% pure.

21. The composition of claim 12, wherein the polypeptide is at least 90% pure.

22. The composition of claim 12, wherein the polypeptide is at least 99% pure.

23. A formulation comprising

a) a therapeutically effective amount of a substantially pure, enzymatically active naturally occuring human plasma hyaluronidase, wherein said polypeptide is at least 60%, by weight, free from the proteins and naturally-occurring organicmolecules with which it is naturally associated and wherein said polypeptide is glycosylated, and

b) a pharmaceutically acceptable carrier.

24. The formulation of claim 23, wherein the carrier is a liposome.

25. The formulation of claim 23, wherein said polypeptide exhibits a specific activity of at least 2×10^5 relative turbidity reducing units per mg protein.

26. The formulation of claim 23, wherein the human plasma hyaluronidase polypeptide is present at a concentration of about 1.5×10^5 turbidity reducing units per milliliter of formulation.

27. The formulation of claim 23, wherein said glycosylated polypeptide is sensitive to N-glycosidase-F treatment.

28. The formulation of claim 23, wherein said glycosylated polypeptide comprises a mannose residue.

29. The formulation of claim 23, wherein said polypeptide further comprises a fatty acid modification.

30. The formulation of claim 29, wherein said fatty acid modification is resistant to phospholipase-C, phospholipase-D, and N-glycosidase-F.

31. The formulation of claim 23, wherein said polypeptide exhibits a specific activity of at least 6×10^5 relative turbidity reducing units per mg protein.

32. The formulation of claim 23, wherein said polypeptide has a relative molecular mass of about 57 kDa as determined by sodium dodecyl sulfate polyacrylamide gel electrophoresis.

33. The formulation of claim 23, wherein the polypeptide is at least 75% pure.

34. The formulation of claim 23, wherein the polypeptide is at least 90% pure.

35. The formulation of claim 23, wherein the polypeptide is at least 99% pure.

36. A formulation comprising

a) a therapeutically effective amount of a recombinant, substantially pure, enzymatically active naturally occuring human plasma hyaluronidase, wherein said polypeptide is at least 60%, by weight, free from the proteins and naturally-occurring organic molecules with which it is naturally associated and wherein said polypeptide is glycosylated; and

b) a pharmaceutically acceptable carrier.

37. The formulation of claim 36, wherein the carrier is a liposome.

38. The formulation of claim 36, wherein said polypeptide exhibits a specific activity of at least 2×10^5 relative turbidity reducing units per mg protein.

39. The formulation of claim 36, wherein the human plasma hyaluronidase polypeptide is present at a concentration of about 1.5×10^5 turbidity reducing units per milliliter of formulation.

40. The formulation of claim 36, wherein said glycosylated polypeptide is sensitive to N-glycosidase-F treatment.

41. The formulation of claim 36, wherein said glycosylated polypeptide comprises a mannose residue.

42. The formulation of claim 36, wherein said polypeptide further comprises a fatty acid modification.

43. The formulation of claim 42, wherein said fatty acid modification is resistant to phospholipase-C, phospholipase-D, and N-glycosidase-F.

44. The formulation of claim 36, wherein said polypeptide exhibits a specific activity of at least 6×10^5 relative turbidity reducing units per mg protein.

45. The formulation of claim 36, wherein said polypeptide has a relative molecular mass of about 57 kDa as determined by sodium dodecyl sulfate polyacrylamide gel electrophoresis.

46. The formulation of claim 36, wherein the polypeptide is at least 75% pure.

47. The formulation of claim 36, wherein the polypeptide is at least 90% pure.

48. The formulation of claim 36, wherein the polypeptide is at least 99% pure.

49. A composition comprising a substantially pure, enzymatically active naturally occurring human plasma hyaluronidase (hpHAse) polypeptide, wherein said polypeptide is at least 60%, by weight, free from the proteins and naturally-occurring organic molecules with which it is naturally associated and wherein said polypeptide is glysolated, and wherein said hpHAse polypeptide exhibits β-1,4-endoglycosidase activity and a pH optimum below pH 4.5.

50. The composition of claim 49, wherein the hpHAse polypeptide exhibits a pH optimum of between about pH 3.0 and about pH 4.0.

51. The composition of claim 49, wherein the hpHAse polypeptide exhibits a pH optimum of between about pH 3.0 and about pH 3.7.

52. The composition of claim 49, wherein said glycosylated polypeptide is sensitive to N-glycosidase-F treatment.

53. The composition of claim 49, wherein said glycosylated polypeptide comprises a mannose residue.

54. The composition of claim 49, wherein said polypeptide further comprises a fatty acid modification.

55. The composition of claim 54, wherein said fatty acid modification is resistant to phospholipase-C, phospholipase-D, and N-glycosidase-F.

56. The composition of claim 49, wherein said polypeptide exhibits a specific activity of at least 6×10^5 relative turbidity reducing units per mg protein.

57. The composition of claim 49, wherein said polypeptide has a relative molecular mass of about 57 kDa as determined by sodium dodecyl sulfate polyacrylamide gel electrophoresis.

58. The composition of claim 50, wherein said polypeptide exhibits a specific activity of at least 2×10^5 relative turbidity reducing units per mg protein.

59. The composition of claim 49, wherein the polypeptide is at least 75% pure.

60. The composition of claim 49, wherein the polypeptide is at least 90% pure.

61. The composition of claim 49, wherein the polypeptide is at least 99% pure.

62. A composition comprising a recombinant, substantially pure, enzymatically active naturally occuring human plasma hyaluronidase (hpHAse) polypeptide, is at least 60%, by weight, free from the proteins and naturally-occurring organicmolecules with which it is naturally associated and wherein said polypeptide is glycosylated, and wherein said hpHAse polypeptide exhibits β-1,4-endoglycosidase activity and a pH optimum below pH 4.5.